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Dynamic changes from depolarizing to hyperpolarizing GABAergic actions during giant depolarizing potentials in the neonatal rat hippocampus

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Abstract

© 2015 the authors. During development, GABA exerts depolarizing action on immature neurons and, acting in synergy with glutamate, drives giant depolarizing potentials (GDPs) in the hippocampal network. Yet, blockade of the GABA(A) receptors transforms GDPs to epileptiform discharges suggesting dual, both excitatory and inhibitory, actions of GABA in the immature hippocampal network. However, the nature of this dualism in early GABA actions is poorly understood. Here we characterized the dynamics of synaptic currents mediated by GABA(A) and glutamate receptors through an estimation of the changes in their conductance and driving forces in neonatal rat CA3 pyramidal cells during GDPs. We found that depolarizing GABAergic and glutamatergic currents act in synergy at the GDPs' onset. However, during the peak of the population discharge, the inward synaptic current was essentially mediated by glutamate receptors whereas GABA currents transiently switched their direction from depolarizing to hyperpolarizing as a result of neuronal depolarization above the GABA(A) reversal potential. Thus, the action of GABA on CA3 pyramidal cells dynamically changes during GDPs from excitatory at the GDPs' onset to inhibitory at the GDPs' peak. We propose that the dynamic changes in GABA actions occurring during GDPs enable GABAergic interneurons not only to initiate the discharge of pyramidal cells but also to control excitation in the recurrent CA3 network preventing epileptiform synchronization.

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Keywords

Development, GABA, Giant depolarizing potentials, Hippocampus, Network, Synchronization